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ON

MYOMA AND FIBRO-MYOMA OF THE UTERUS

AND

ALLIED TUMOURS OF THE OVARY.

BY

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ON MYOMA AND FIBRO-MYOMA OF THE UTERUS AND ALLIED TUMOURS OF THE OVARY.

By ALBAN DORAN.

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(*Abstract.*)

MYOMA of the uterus is very common, fibroma of the ovary rare. The study and comparison of these tumours involve the distinction between true muscle-cells and certain cells found in fibrous tissue and in sarcomata. Some pathologists declare that there is no true distinction. Certain recognised types, such as the plain muscle-cells of the walls of blood-vessels, and the muscle-cells of the pregnant, non-pregnant, and foetal uterus, are compared in this memoir with the cells of tumours evidently made up of fibrous tissue, or evidently sarcomatous, or otherwise malignant. Each type is illustrated not only by verbal descriptions but also by accurate drawings executed by a competent artist.

The histology of the uterine wall is not a very complicated subject. Plain muscle-cells mixed with more or less connective tissue, and arranged in bundles, are the chief constituents of the wall, and extend not only to the tube but also to the round ligament and the ovarian ligament, true processes of the uterus. A non-malignant tumour made up of muscle-cells very commonly develops in the uterine walls, or may form in one of the uterine processes. This is myoma of the uterus. From the uterine connective tissue white fibre may be developed, hence the origin of fibro-myoma of the uterus. Klebs' and Kleinwächter's theories are discussed. The muscle-cells of a myoma are usually larger than those of the uterus in which it grows. Hence in a myoma removed during pregnancy they appear very large. The comparison of the muscle-cells with the smaller cells

of similar appearance found in the white fibrous tissue in a fibro-myoma is important, especially in relation to suspected cases of myoma of the ovary.

The histology of the ovarian stroma in woman is, on the other hand, very unsettled. Ideas on the subject are too often gleaned from the study of animals' ovaries. Harz's researches show how this study may lead to grave fallacies. The tissue of the hilum and parenchyma is described, and allowance is made for changes in the follicles (corpora fibrosa of Patenko, &c.). True fibrous tissue is naturally abundant in the tissue of the hilum (paroöphoron); this fact is enough to account for fibroma of the ovary. Muscular tissue is found amidst the parenchyma of the ovary in the coats of its vessels, and also in free bundles derived from the ovarian ligament, a process of the uterus. The connective tissue of the ovary around the follicles (stroma of the parenchyma, as distinguished from the tissue of the hilum) is variable in character, but as a rule of a young type. Common changes due to inflammation must be borne in mind.

Fibroma of the ovary is a well-known but rather rare disease. Its development is accounted for above. Sarcoma of the ovary is not so rare, owing probably to the frequent abundance of "young" connective tissue. Specific spindle-cells of a sarcoma are compared with the connective-tissue cells in fibroma. The existence of fibro-myoma of the ovary has been disputed. As muscular tissue naturally exists in the ovary the development of myoma can be accounted for. The difficulty of distinguishing muscle-cells from certain cells in the other tumours described in this paper is admitted, yet, by comparing a fibro-myoma of the uterus with a tumour of similar characters growing in the ovary, it appears that this distinction can be made, and hence there is little doubt that a fibro-myoma may develop in the ovary. At least, plain muscle-cells, the fusiform cells of fibrous tissue, and the specific spindle-cells of a sarcoma, may in many cases be distinguished from each other.

MYOMA of the uterus is very common, fibroma of the ovary is rare. This fact is universally admitted, yet the study of myomata and fibromata includes a most difficult task,—the distinction between true muscle-cells and cells

found in fibrous tissue and in sarcomata. Some authorities assert that no such distinction can be defined; Virchow, Billroth, and Winiwarter are especially doubtful on this point. The question must be solved, firstly, by the labours of general histologists and pathologists, who have yet to trace more accurately than heretofore the differentiation of indifferent embryonic tissues, and to determine how far we can depend upon the effects of staining materials. Secondly, this question demands for its solution a line of research which this memoir is designed to encourage. Certain recognised types, such as the muscle-cells of the walls of blood-vessels, and the muscle-cells of the pregnant, non-pregnant, and foetal uterus, will be compared with the cells of tumours evidently made up of fibrous tissue, or evidently sarcomatous or otherwise malignant. Through the known we may succeed in determining the unknown. The cells and their arrangement must be kept before the eye whilst they are being talked about. For this reason I exhibit this evening a series of microscopic preparations. I further submit to the Society a collection of drawings of these preparations as seen with a one-eighth inch objective. These drawings were executed under my superintendence by Mr. Lewin, a painstaking and accurate artist.

I shall employ the term "muscle-cell" throughout the monograph, the expression "muscular fibre" being confusing. Non-striated muscular tissue and leiomyoma is in every case understood, unless the terms "striated muscular fibre" and "rhabdomyoma" are employed. Again, by "spindle-cells" I mean the cells of a true spindle-celled sarcoma only, by "fusiform cells" any cells which are spindle-shaped. As to rhabdomyoma or striated muscular tumour of the uterus, only seven cases have been described. It always takes the form of a racemose tumour of the cervix, distinctly resembling hydatid mole, and is essentially malignant. The cells are very large, fusiform, and, as Dr. Pernice has discovered, distinctly marked with transverse striæ. Thus they resemble striated muscular tissue in early foetal life; in fact, they represent early and

extreme histological specialisation, and hence the subject of uterine rhabdomyoma is foreign to this monograph, as I confine myself to comparisons between far more generalised structures, namely, fibrous tissue, spindle-cells of sarcomata, and plain muscle-cells. Otto Weber has found striated muscle-cells in uterine polypi, possibly incipient forms of the racemose inalignant tumour of the cervix. He believes that they arise by direct conversion of plain muscle-cells. The subject is ably treated by Dr. Pernice ("On Racemose Myosarcoma Striocellulare Uteri," 'Virchow's Archiv,' vol. cxiii, part 1).

I shall begin by a consideration of MYOMA OF THE UTERUS. This subject is in many respects easier than the study of ovarian new growths. The structure of the uterine wall is fairly constant, even in its changes, from early foetal life to old age. In sections from a four-months' foetus I found that the muscle-cells were already well formed. Each cell was of the spindle shape seen in the non-pregnant adult uterus, and tapered gradually; the nucleus was elongated, but wider than in the adult. Tournieux and Legay* and Cadiat† represent the foetal uterine muscle-cells after the pattern just described, but do not figure any bulging of the nuclei. In sections from a seven months' foetus the muscle-cells near the fundus were well developed, and the nuclei were of the form which they assume in the adult. Towards the cervix and around large vessels, the muscle-cells seemed younger than elsewhere. In Fig. 1, representing a section of the uterus before puberty, the muscle-cells forming the middle coat of the blood-vessels closely resemble the same cells in well-developed uterine tissue, whilst the muscular tissue outside the blood-vessels is less characteristic, the nuclei being stout, though elongated, and the remainder of each cell hardly distinguishable. The gradation from these nuclei to

* "Mémoire sur le développement de l'utérus et du vagin envisagé principalement chez le fœtus humain," 'Journal de l'Anatomie et de la Physiologie,' tome xx, 1884; see especially pl. xxv, figs. 24—26.

† "Mémoires sur l'utérus et les trompes," *ibid.*, see pl. xxvii, fig. 12.

fully developed uterine muscle-cells was evident in the specimen now described. The presence of the youngest tissue nearest to the vessels may indicate that Kleinwächter's theory, which will presently be quoted, applies to the development of the uterus as well as to the formation of myomata.

The natural variations in the amount of connective tissue in the uterine walls, and the changes in the muscle-cells during pregnancy, are also tolerably well understood. The chief difficulty in the study of the histology of the uterus lies in the intricate arrangement of its fibres. Hence it is all the more important to study the individual cell.

We may take for granted, firstly, that the walls of the uterus are made up of plain muscle-cells, with a varying amount of connective tissue, which is never so purely fibrous as the substance of a fibroma. Secondly, that the muscular tissue of the walls extends to the round ligament and to the ovarian ligament which are true processes of the uterus.* Thirdly, that a pathologically innocent tumour, made up of plain muscle-cells with a varying amount of fibrous tissue very frequently develops in the uterus and may form in the round ligament (see Mr. Stanley's specimen in the Museum of the Royal College of Surgeons, Path. Series, No. 386) and in the ovarian ligament (author's case, 'Trans. Path. Soc.,' vol. xxxviii, p. 245).

The morbid anatomy of uterine myoma is well known. Nothing need here be said about its submucous, interstitial, subperitoneal, and polypoid varieties. Gusserow ("Die Neubildungen des Uterus," Billroth and Luecke's 'Deutsche Chirurgie,' Lieferung 57) has little to say on the histology of myoma. In relation to the fibrous element, he observes that the more the fibro-myoma is a simple hypertrophy or rather hyperplasia of the uterine tissue as in pregnancy, but localised instead of general, the more will the plain muscle-cells preponderate, and the growth will be a pure myoma; the more a kind of fibrous induration of the

* I put aside for the present the significance of muscle-cells in the utero-sacral and broad ligaments, and the continuity of rows of muscle-cells proceeding from the uterus along the ovarian ligament into the ovary.

interstitial connective tissue takes a part at the beginning or in the course of development in pushing aside the muscular fibrils, the more nearly will the growth be a pure fibroma. Such observations are philosophical rather than scientific. The cystic and degenerative changes which many "fibroids"* undergo are well known.

The development of muscle-cells and their alleged proliferation are questions more to the purpose in this memoir. That muscle-cells proliferate in the adult has not been proved; I can find no evidence of the proliferation theory except in books. Klebs noticed that the formation of muscular tissue went on simultaneously with the development of vessels and the consequently freer access of nutrition. Dr. Kleinwächter† appears to have made an important discovery, suggested perhaps by the above theory of Klebs. He examined incipient, almost microscopical myomata, which he found under the serous coat of the uterus in the post-mortem room. In these minute growths he found the muscle-cells larger, as a rule, than in uterine tissue. The incipient myoma was more or less circumscribed, fusiform or pyriform, with a tapering pedicle, a point of special importance. The capillaries near the myoma were surrounded by parallel rows of round-cells, which were sometimes undergoing proliferation and were smaller in diameter than the neighbouring muscle-cells. This process involved the destruction of the capillary. Dr. Kleinwächter traced the round-cells developing into muscle-cells through an intermediate fusiform type. I have already suggested that this is possibly the manner in which the normal muscular tissue of the uterus is developed. In fig. 1 the capillaries are seen to be surrounded by nuclei rather stouter than those of well-formed muscle-cells, and certainly less elongated. I find that the further the section is examined away from the vessels, the more the stout nuclei are replaced by muscle-cells.

* By this term I mean to designate all myomata, fibro-myomata, and cystic myomata of the uterus.

† "Zur Entwicklung der Myome des Uterus," 'Zeitschrift für Geburtshilfe und Gynäkologie,' Band ix, p. 68.

*"Kelly & Ballen 'Myomata of the Uterus' 1902
p. 430-434 could not find any conclusive
evidence that a myoma develops around blood vessels*

*a B: a
capillary has
no muscular
coat*

Dr. Kleinwächter found that the process above described ended by destroying the capillary, which ultimately remained as the tapering point of the myoma. A cluster of minute myomata corresponded to the conversion of several branches of a capillary into new growths. In a case of death a few hours after labour he found a minute uterine myoma, the cells of which had shared in the hypertrophy of pregnancy, but to a less degree than the normal uterine tissue. The round-cells were abundant, and were not only massed round the vessels in the myoma, but also lay between the fasciculi and in the connective tissue of the capsule. I shall say more, presently, on the hypertrophy of the muscle-cells of a myoma in pregnancy.

MYOMA OF THE NON-PREGNANT UTERUS is made up of muscle-cells resembling those which compose the uterine wall.* The fibres interlace in all directions and in many degrees of density. Fig. 2 is a good sample of this kind of tumour. It grew in the ovarian ligament, a process of uterine tissue, and the uterine walls were infested with similar growths.† In the drawing the field is entirely covered with small, very elongated muscle-cells. No other kind of cell nor any fibrous or vascular structure can be seen. The muscle-cells are mostly arranged in rows which branch laterally, suggesting, perhaps, their original development from capillaries. It may be noted that the cells in this drawing much resemble the muscle-cells in the coats of small vessels (fig. 1). They are much smaller than the muscle-cells of a myoma in pregnancy (fig. 3), and much larger and more distinct than the fusiform cells or nuclei which are mixed with the wavy fibres of an ovarian fibroma (fig. 5).

* Throughout this memoir I have endeavoured to avoid all comparisons, unless based on direct evidence gained by the examination of specimens. I regret that obvious reasons prevent me from supplying sketches of a large number of sections of normal uterine tissue during foetal life, adult life, and pregnancy. All the comparisons between morbid and healthy structures are based on the careful inspection of numerous sections, of the kind just indicated, in my own collection, and in that of Dr. W. S. A. Griffith.

† For a full account of the case see 'Trans. Path. Soc.,' vol. xxxviii, p. 245.

MYOMA OF THE PREGNANT UTERUS.—I am able to exhibit this evening a beautiful microscopical section of a myoma, removed, together with the entire uterus, at about the fourth month of pregnancy. Dr. Bantock was the operator, and the patient made a good recovery. The myoma was situated in the posterior wall of the uterus, bulging high upwards and far backwards. Its anterior and upper part was very soft and vascular, its posterior part was much firmer. From this firmer portion the section (fig. 3) was made. A uniform collection of large elongated cells covers the field. Each cell is flattened and tapers very gradually at each end to a long, fine point. The nuclei, which are deeply stained, resemble the cells in shape, some are very tortuous; in parts of the specimen whence fig. 3 was drawn I observed that the cells bore perfectly oval, though elongated, nuclei. In a section from the softer part of the same tumour the same large cells were found, but there were spaces filled with very fine connective tissue between the bundles of muscle-cells. I could not detect any bundles of well-formed white fibres, such as are seen in connective tissue in healthy structures, in tendons, and in fibromata.

The great size of the muscle-cells is the chief feature of interest in this case. They are not merely somewhat larger, they are far larger than the same cells in the walls of a pregnant uterus. I have recently compared the preparation above with some fine slides showing the muscular tissue of a uterus from a fatal case of Cæsarean section, and also with other slides showing the uterine tissue, from a case where death occurred from puerperal septicæmia on the tenth day after labour. All these preparations are in Dr. Griffith's collection. In none do I find any muscle-cells approaching in magnitude those depicted in fig. 3.

At the same time, the size of the muscle-cells, may, I think readily be explained. The tumour is muscular, like the uterine walls; the uterus had undergone the characteristic changes which occur in pregnancy, and the tumour had participated in those changes. The proportion between

the muscle-cells in the normal tissue and in the new growth was maintained in this case, that is to say the myoma cells were larger than the uterine tissue cells, as in non-pregnant cases. I do not think that there is sufficient reason to suppose that the tumour was sarcomatous in the sense implied by von Winiwarter in the fourth edition of Billroth's 'General Surgical Pathology and Therapeutics.'* The above explanation appears perfectly natural, nor had the tumour any of the clinical characters or physical appearances of what may be termed a semi-malignant fibroid, or of Pernice's racemose rhabdomyoma of the cervix.

FIBRO-MYOMA OF THE UTERUS.—By this term is implied a uterine tumour where groups of muscle-cells are blended with, or completely separated by, conspicuous tracts of fibrous tissue. A small amount of young connective tissue as seen in the uterus is never absent from a pure myoma; in fibro-myoma we see well-defined wavy bands of white fibre. Microscopically no two sections of fibro-myoma of the uterus look alike. Sometimes wide bands purely made up of muscle-cells predominate; sometimes the field is covered with white fibre, resembling that of which a fibroma of the ovary (fig. 5) is entirely composed. Lastly, the muscle-cells, or at least structures resembling them in size and appearance, may be intimately connected with the fibrils which make up the fibrous bands. This latter condition, well indicated in fig. 4, which represents a section of a pedunculated subperitoneal "fibroid," must be borne in mind. For in this case there can be no doubt of the uterine origin of the tumour and therefore practically no doubt about the presence of muscle-cells. In examining

* "One reason for distinguishing this tumour (uterine fibroid) from sarcomata is that, in the uterus, rapidly growing recurrent tumours develop, in whose older parts the structure of fibroma predominates, while the younger portions contain quantities of spindle-cells—true sarcoma cells. Clinically these tumours do not act like the much more frequent myomata, but like sarcomata. Some pathologists assume that in these cases there has been a development of a sarcoma in a fibroma; but it is more natural, from the predominance of the signs, to class these tumours as sarcomatous" (Dr. Hackley's Translation, 1884).

a solid tumour of an ovary, an organ which contains but few muscle-cells, we may come across a similar condition where large fusiform cells (differing from the specific "spindle-cell" of a sarcoma) are blended with fibrous tissue; in other words we can recognise what must fairly be considered as fibro-myoma.

Of all "fibroids" fibro-myoma is the commonest form, but I do not think that it is so frequent in proportion to pure myoma as is generally supposed. In many soft "fibroids" (as in the softer part of the myoma removed during pregnancy, already described) connective tissue abounds, but connective tissue is not fibrous tissue. When large, fibro-myomata are very tough; young, minute "fibroids" are usually, if not always, pure myomata with or without connective tissue; as that tissue, as well as pure white fibre, may readily undergo various kinds of degeneration, it is not easy to say whether myoma or fibro-myoma is the more likely to break down in parts or to calcify.

FIBRO-SARCOMA OF THE UTERUS.—This disease does not come within the scope of this memoir as its sarcoma cells appear, according to all specimens which I have seen, to bear no resemblance to muscle-cells and to the small connective-tissue cells with which muscle-cells may be confused. Round-cells predominate and are generally large. The physical characters differ from those of the solid, tough tumours at present under consideration (see Museum of the Royal College of Surgeons, Path. Series, No. 4672). Still more different in character is the diffuse sarcoma of the endometrium. Gusserow (loc. cit.) devotes an important chapter to sarcoma of the uterus.*

MYOMA OF THE OVARIAN LIGAMENT.—I have already described this ligament as a process of uterine tissue. A myoma in its substance (fig. 2) is practically a myoma of

* Pernice's rhabdomyoma of the cervix ("racemose myosarcoma strio-cellulare uteri") becomes truly sarcomatous when recurrent. The cells then appear very large and multiform, often bearing large nuclei. No trace of transverse striæ can be detected (loc. cit.).

12) F. Spaeth (Hamburg). Ein Fall von Fibroid des Eileiters.

(Zeitschrift für Geburtshilfe und Gynäkologie Bd. XXI. Hft. 2.)

Bei einer Frau, die an häufigem Erbrechen und ständigen Schmerzen in der linken Seite litt, wurde durch Laparotomie eine Geschwulst entfernt, die der linken Tube angehörte und durch peritonitische Adhäsionen verwachsen war. Die Tube war wesentlich verkürzt und ging nach einem Verlauf von 1 cm vom Uterus aus in eine Geschwulst über, in die das abdominale Ende aufgegangen war, und die aus der gleichmäßig verdickten (4 cm) Tubenwand bestand. Mikroskopisch zeigte die verdickte Wandung genau das Bild eines Fibromyoms, entzündliche Processe waren nicht vorhanden. Da die Tuben, wie der Uterus aus den Müller'schen Gängen hervorgegangen sind, so hält sie S. für die Entwicklung einer solchen Neubildung für gleichwerthig.

Cario (Göttingen).

mäßig häufig der Fall, so dass man zu der Annahme gedrängt würde, dass polypoiden Theile der Geschwulst durch die Entfernung der Anhänge leicht beeinflusst werden. Benton bemerkt, dass er ebenfalls mehrfach Fälle beobachtet habe, in welchen die Placenta nach Absterben der Frucht weiter gewachsen. In einem Falle fand sich letztere weit von der Placenta entfernt ohne Verbindung derselben, sicherlich seit drei oder vier Monaten abgestorben, und die Größe von der Größe einer solchen am Ende der Schwangerschaft.

Routh bemerkt, dass häufig mit Myomen zugleich Polypen bestanden, dass die Blutung aufhöre, sobald letztere entfernt wären; daher solle man mit Entfernung der Anhänge die Behandlung beginnen.

Sitzung am 11. Juni.

Tait hält einen eingehenden Vortrag über Wiederherstellung des Pfortaders. Er bespricht zunächst wie er nach manchen Misserfolgen allmählich

the uterus. Two matters of importance are associated with the term "ovarian ligament." In the first place, it has been described as expressing a fold of peritoneum enclosing a few muscular fibres, when in reality it should signify a stout band of muscular fibres which forms a peritoneal fold, but that fold is not the ligament. Secondly, being made up of muscular fibres, it is natural for us to trace the destiny of the muscle-cells on the ovarian side, for their existence in the organ at the other end of the ovarian ligament, namely, the uterus, is evident. The ligament, I find, joins the parenchymatous part of the ovary (oöphoron) rather than the tissue of the hilum (paroöphoron). Do the structures so like muscle-cells which are found in the stroma of the ovarian parenchyma actually proceed from the uterus, or are those cells simultaneously developed along the ovarian ligament and in the organs at each of its extremities? I cannot find any account of the development of the ovarian ligament which would explain this point. The embryologists alone can solve the problem, which must be solved before we can draw trustworthy inferences from the study of ovarian histology.

MYOMA OF THE ROUND LIGAMENT is, again, a condition readily explained, when we remember that the ligament in question is a process of the uterus. Considering that the Fallopian tube is, morphologically, a part of the uterus and contains dense layers of muscular tissue in its walls, it is, perhaps, remarkable that we do not find authentic cases of MYOMA OF THE FALLOPIAN TUBE in the archives of pathology. Sir J. Y. Simpson's case of fibroid tumour of the Fallopian tube, of "a size equal to that of a child's head," has been repeatedly quoted. A glance at fig. 93 in his 'Clinical Lectures on the Diseases of Women,' 1872, p. 540, will show that the tumour which was attached to the upper aspect of the tube by a pedicle several inches long, could hardly have arisen from the walls of the tube, which appear perfectly normal. The tumour was no doubt developed in the reflexion of the broad ligament over the free border of the

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Trans. & Dis.
Obstet. Soc.
Vol. IV. p. 195.
also Kleinwächter
Zeitschr. f. Geburtsh.
Vol. VIII, 1892.

tube. Cysts often appear in the same position (see "Broad Ligament Cysts above the Fallopian Tube," 'Trans. Path. Soc.,' vol. xxxvii, p. 348). Chiari has recently shown ("Zur pathologischen Anatomie des Eileiterkatarrhs" 'Prager Zeitschrift für Heilkunde,' vol. viii) that the nodules occasionally found at the uterine end of the tube* are not myomata, as others have supposed, but products of chronic tubal catarrh.

The possibility of MYOMA OF THE BROAD LIGAMENT is comprehensible, as there are layers of muscular tissue between the folds of that ligament which hypertrophy in some cases of intraligamentary tumours, cystic or solid. This hypertrophy accounts for the dull red colour of the surface of many intraligamentary tumours which causes them to look like uterine myomata, even when they happen to be thin-walled unilocular cysts. The relations of a tumour of this class must be accurately determined before it is written down as "myoma of the broad ligament." Some ovarian and uterine and all parovarian tumours burrow between the folds of the ligament, and certain cystic non-parovarian growths must likewise be excluded. Nevertheless I assisted Dr. Bantock, in the autumn of 1887 in removing two solid tumours which grew between the folds of the broad ligaments and appeared to be unconnected with the uterus or ovaries. The microscopical sections which I possess show abundance of white fibrous tissue, collections of muscle-cells and a homogeneous almost transparent matrix. I think that each tumour was a true fibro-myoma of the ovarian ligament resembling a soft uterine "fibroid," its peculiar appearance being the result of œdema. Mr. Bland

* These nodules have been discovered in cases of ectopic gestation, and reasonably suspected to be the cause of that pathological condition. Mr. Allport ("Extra-uterine Fœtation," 'Lancet,' vol. ii, 1845, p. 430) describes a case of rupture of a tubal cyst at the fifth month. "The right angle of the (uterine) cavity was obliterated, and we could not detect any orifice leading to the right Fallopian tube, which appeared to be impervious as far as the sac, at its junction with which lay a small fibrous tumour about the size of a horse-bean. A similar growth, as large as a nutmeg, was attached to the walls of the sac." The left tube was healthy.

Sutton, who also examined the tumours, believed that they were of the fibroma-molluscum type described by Virchow.

THE CONNECTIVE TISSUE OF THE OVARY.—The study of this subject is as difficult and complex as the study of the uterine tissue is relatively easy and simple. Industrious pathologists frequently start with erroneous opinions about the human ovary. At the medical schools, in France and Germany as well as in this country, the histology of the ovary is too often taught from specimens taken from the lower animals. We might as well teach human osteology from a kangaroo's skeleton. In a most important monograph,* Dr. Harz has demonstrated, by careful examination of the ovaries of many mammals, that the relation of the hilum tissue or paroöphoron, which bears ingrowths from the Wolffian ducts, to the follicle-bearing parenchyma, differs greatly even in mammals of the same order. Thus in the pig no ducts are found in any part of the ovary. In the guinea-pig, so often sacrificed on the altar of pathology, the ducts permeate the entire stroma; and so they do in the ovary of the American monkey *Cebus*, whilst the Wolffian epithelium is much less abundant in the stroma of another well-known American monkey, *Hapale*, the marmoset.

Yet the investigator's difficulties will not be at an end after a long and exclusive study of human ovaries. In the ovary of the human foetus up to the third month, the connective tissue is almost inextricably mixed up with the primitive follicles and undergoes complex changes, described by Balfour† and Foulis,‡ in relation to the development of the follicles. These changes make it dangerous to draw comparisons between the very heterogeneous cells of

* "Beiträge zur Histologie des Ovariums der Säugethiere," 'Archiv für mikroskopische Anatomie,' Bd. xxii, 1883.

† "On the Structure and Development of the Vertebrate Ovary," 'Quart. Journ. Micros. Sci.,' vol. xviii, 1878.

‡ "The Development of the Ovary and the Structure of the Ova in Man and other Mammalia," 'Journ. of Anat. and Phys.,' vol. xiii, pt. 3, p. 353.

the ovarian stroma and the muscle-cells of the uterus in foetal life. The muscle-cells in the uterine walls have almost acquired their adult form, as I have already stated. The ovarian connective tissue varies greatly in appearance from foetal life up to puberty, as I find after the examination of a considerable number of children's ovaries. During active sexual life all kinds of imperfectly understood normal and pathological conditions may be present. The follicles and the muscular coats of the blood-vessels remain, as far as I can make out, the only constant histological elements. The follicles undergo numerous progressive and retrograde changes. By progressive changes I mean the formation of corpora lutea, and include the degeneration of those bodies, an extremely complicated subject not to the point in this memoir, for corpora lutea cannot develop muscle-cells. By retrograde changes of the follicles I refer to the degeneration of those which have never matured, and so never had the chance of becoming corpora lutea. Whole groups of follicles may degenerate before ripening.* In my opinion these groups may again develop, in a morbid direction, forming the true multilocular ovarian cyst, but I can find no evidence that they ever become myomata or fibromata. The cysts found in solid ovarian tumours bear no signs of follicular origin. The blood-vessels of the ovary are of more direct importance in relation to fibroma and myoma of the ovary. The arteries have very thick walls, with stout muscular coats. They may certainly become obliterated under various morbid influences, and then the fate of their muscle-cells must be taken into account. I have detected large fibres made up of muscle-cells in diseased ovaries, where the arrangement of the fibres left little doubt that they represented obliterated blood-vessels.

Patenko ("Ueber die Entwicklung der Corpora Fibrosa

* Janosik has found that in all ovaries an infinite number of follicles undergo atrophy, many beginning to decay during their earliest stages. The atrophic process varies considerably in individual follicles ('Sitzungsberichte d. kaiserl. Akad. d. Wissenseh.,' vol. xcvi, pt. 3, 1888).

in Ovarien," 'Virchow's Archiv,' vol. lxxxiv, 1881) has satisfactorily shown that the curious little round fibrous bodies often found in ovaries at necropsies are of purely follicular origin. These "corpora fibrosa" represent sclerotic changes and never form fibromatous tumours. The arteries undergo sclerosis and in the course of their degenerations the muscular cells of the tunica media disappear through fatty metamorphosis and are replaced by granulation elements which simultaneously fill the adventitia. The white laminated bodies (*geschichtete Körper*) found amongst the sclerosed vessels are apparently of fibrinous intravascular origin. Patenko admits that fibromata cannot develop from his corpora fibrosa, and it is evident that myoma could not arise from them. Above all, they bear no resemblance, in any stage, to fibrous tissue.

Putting aside the follicles and the blood-vessels, the parenchyma must be considered. The paroöphoron or tissue of the hilum normally contains much true fibrous tissue, quite enough to account for fibroma of the ovary. Its Wolffian elements cannot give origin to that disease; they are epithelial bodies lining tubes and are the source of the papillomatous ovarian cyst which often burrows into the broad ligament. The normal character of the stroma of the parenchyma or ovary proper is hard to determine on account of the difficulty of distinguishing purely parenchymatous changes from the results of the degeneration of follicles and of blood-vessels. In the infant this stroma is very scanty. In ovaries from young women of eighteen or twenty great quantities of atrophied or degenerated follicles and corpora lutea are to be found. Nevertheless, there is a stroma of connective tissue, always rather "young" in character, with much homogeneous matrix. The fibres are scattered, never forming stout wavy bundles. I have never failed to detect bodies bearing all the appearances of muscle-cells. These bodies do not run in regular strands or fibrils, or if they do, they appear to proceed from the inner limits of the ovary as though they came from the uterus along the ovarian ligament. Sometimes these muscle-cell-like bodies

are intimately blended with the wavy bands of fibrous tissue in the parenchyma.

In the large succulent ovaries found in some cases of chronic oöphoritis, muscle-cells are often found in great abundance, as in two specimens in my own collection, but the evidence is strong that these cells represent obstructed vessels. Ovaries of this kind do not appear to become solid tumours; that they may develop into large cystic tumours is, I believe, more probable. A large fleshy ovary is very frequently discovered as the fellow of an ovarian cyst during ovariectomy.

From the above observations it may be seen that fibrous and muscular elements at least exist in the ovary, the former as a tissue, the latter rather as part of the vessels or as a continuation of the ovarian ligament. We have enough to account for fibromata and myomata of the ovary. I shall now turn to a consideration of tumours of those two classes.

FIBROMA OF THE OVARY.—The existence of this tumour is almost universally admitted. Dr. Coe has written a valuable monograph on the subject.* I have examined microscopically at least three solid ovarian tumours which appeared as though entirely made up of white fibrous tissue, as well as many others where that tissue predominated, whilst cellular elements were also present in sufficient abundance to suggest sarcoma. The bilateral, firm, solid tumours of the ovary are generally sarcomatous and give rise to clinical symptoms of malignancy, such as ascites, before they attain large proportions (see Dr. Cullingworth's case, 'Trans. Obstet. Soc.,' vol. xxi, 1879, pp. 276, 314). Some of the small fibrous tumours of the ovary described in the Pathological Society's 'Transactions' and elsewhere were probably examples of the effects of chronic oöphoritis or of the abundant formation of corpora fibrosa, already noted. Few of these cases were true fibromata. I have given reasons why it is perfectly simple

* "Fibromata and Cysto-fibromata of the Ovary," 'Amer. Journ. of Obst.,' vol. xv, 1882, pp. 561, 858.

to show that fibromata of the ovary may arise independently of any similar uterine growth, as Dr. Coe has already proved. In none of the specimens which I have examined was there any uterine tumour.

A good example of a pure fibroma of the ovary was our President, Dr. John Williams' specimen; its microscopical characters were reported by Drs. Galabin and Herman and myself in the Society's 'Transactions,' vol. xxix, 1887, p. 513. Fig. 5 is a fine drawing, by Mr. Lewin, of a large fibroma of the ovary removed by Mr. Knowsley Thornton on July 16th, 1884, from a woman aged twenty. She had married when fifteen years of age and had borne no children. A very long abdominal incision had to be made before the tumour could be extracted. The pedicle was long and narrow; the relation of the tube and broad ligament proved clearly that the tumour was ovarian. The uterus was healthy, the opposite ovary small and infantile.*

The section drawn in fig. 5 was made for me by Dr. Vincent Harris in the Physiological Laboratory of St. Bartholomew's Hospital. Characteristic wavy bundles of true fibrous tissue abound; in other sections they were even more closely packed. Small, elongated, fusiform nuclei lie in the bundles of fibres, running invariably in the long axis of the fibres. Between the bundles, sparingly distributed, are small round-cells with oval nuclei such as are to be seen in fibromata in other structures. The sinuous bands of fibres contrast with the straighter rows of muscle-cells seen in myomata of the uterus.

The fusiform nuclei must be remembered, when this kind of tumour is compared with a myoma or a sarcoma of the ovary or uterus. They are certainly found in fibromata of other organs. Whether these nuclei may represent a type

* The after-history of this case, which Mr. Thornton has kindly obtained for me, is of great interest. Previous to the operation sexual desire appears to have been absent. The ovary which was left behind was found, as above stated, to be infantile. After recovery the instinct rapidly developed; the patient left her husband and bore a child to another man. Ultimately she returned to her home, and in February, 1888, she was in good health; there was no sign of return of the tumour.

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1904 Removal of fibroma of ovary Griffiths
1st case removed, 1 lb. Cystic tumour removed
months after op.

of tissue which has been or may become muscular fibre, is an important question. The small round-cells with oval nuclei seen in fig. 5 must be distinguished from bundles of fibres divided transversely. Their nuclei are too stout to represent fusiform nuclei divided in that direction. Mr. Lewin has taken care, as I can bear witness, to draw them accurately. These round-cells are very unlike muscle-cells. More consistently with the appearances of the cells in sarcoma of the ovary (fig. 6) and with modern pathological doctrines, they represent what, if they predominated universally over the fibres, would constitute a true sarcoma.

The tissue of this fibroma is much "older"* than the scanty fibrous tissue of a healthy ovary. Hence probably the greater frequency of sarcoma over fibroma in the ovary. We can understand why fibromata should grow from fibrous periosteum. But connective-tissue tumours are usually of a younger type than the tissue of the structures whence they grew. Therefore from the ovarian stroma, where the connective tissue is normally almost embryonic, a sarcoma is more likely to develop than a fibroma. The fibrous tissue of true cancer of the ovary† must be kept out of consideration at present, as it is a new growth secondary to the cancer itself.

SARCOMA OF THE OVARY.—This disease must now be considered, as the question of the embryonic character of normal ovarian stroma has just been discussed in relation to fibroma. Only in respect to fibroma and leiomyoma need I enter into any description of ovarian sarcoma. I will put aside all those soft malignant ovarian tumours which on microscopical examination present the characters of round-celled, spindle-celled, mixed or alveolar sarcoma,

* Cornil and Ranvier ('Manual of Pathological Histology,' vol. i, second edition, English translation) state that "there are generally no elastic fibres in fibroma, the tissue appearing to be *the purest form of fibrous tissue*. This is an important point."

† I have figured a good specimen in 'Clinical and Pathological Observations on Tumours of the Ovary, Fallopian Tube, and Broad Ligament,' fig. 25, p. 103.

nor need I dwell on the pseudo-melanotic characters of slow-growing sarcomata self-stained through minute capillary hæmorrhages.* I shall confine myself to a consideration of the microscopical appearances of the least malignant form of sarcoma, where there is more than a trace of a fibrous stroma, so that I may demonstrate to what extent the sarcoma-cells amongst the fibres resemble the cells of old connective tissue or the true muscle-cells of a myoma. A spindle-celled sarcoma alone need be taken into account, for the other kinds of cell, just mentioned, are spindle-shaped, therefore they must be, in one respect, like one form of sarcoma cell. Once more, I must add that specimens of spindle-celled sarcoma where a trace at least of fibrous stroma is present are the most important. A pure spindle-celled sarcoma has none of the physical characters of a myoma or fibroma, but a sarcoma partially mixed up with fibrous tissue possesses all these characters.

I have shown a section from a tumour which caused the death of a patient under the care of Sir Spencer Wells in March, 1880. Malignant cachexia was marked, so that no operation was performed. The patient died on May 3rd, 1880. A soft mass replaced the left appendages and adhered to the fundus and body of the uterus. I examined it and found it to be a sarcoma of the left ovary. The greater portion of the tumour, including part of the section whence fig. 6 was drawn, was made up of large round-cells, closely mixed up with a scanty, delicate, fibrous stroma. This stroma formed trabeculæ enclosing round spaces which had no epithelial lining and the cells lay in the trabeculæ, not in the spaces. In other parts, however, most characteristic spindle-cells predominated. I have chosen a point where these spindle-cells are present, and blend with the fibrous stroma, (fig. 6). Fusiform cells with large oval or smaller fusiform nuclei are seen in abundance. These cells are intimately connected by their tapering extremities with the delicate fibrous stroma. Their arrangement suggests

* I have already explained why I deem it unnecessary to dwell on the subject of striated muscular tumours of the uterus.

homologies with the small round-cells seen between the bundles of fibres in the fibroma of the ovary (fig. 5). On the other hand, if compared with any of the drawings of myomata, it will be seen at a glance that there is no close resemblance between a spindle-cell from a sarcoma and a muscle-cell. In fact, fig. 6 represents young connective tissue from a tumour mostly made up of even younger tissue. Each cell is oat-shaped rather than fusiform, and its nucleus is either oat-shaped or almost spherical. The muscle-cell is more truly fusiform, and its nucleus is either staff-shaped or else forms a very elongated oval body.

FIBRO-MYOMA OF THE OVARY.—The existence of a pure myoma of the ovary is very doubtful, but I believe that fibro-myoma of that organ is not rare. I have already spoken of the sources of muscular fibre in the normal ovary. Whether there be muscle-cells diffused over the stroma of the ovary, or whether the only muscle-cells found within the limits of the ovary be those forming the middle coat of the arteries or those which represent the ovarian extremity of the ovarian ligament, matters little, when we consider the suspected tumour itself. These questions, already discussed in this memoir, concern its origin rather than its structure. Rhabdomyoma or striped myo-sarcoma may develop in connection with the kidneys, where there is naturally no striped muscular tissue; Cohnheim considers that the new growth is teratological in this case, and the question is fully considered in Mr. F. S. Eve's paper on "Specimens of Tumours composed of Striped Muscle and Sarcoma Tissue (Striped Myo-sarcoma), connected with the Kidneys" ('Trans. Path. Soc.,' vol. xxxiii, 1882, p. 312). There is no need to resort to teratology in the case of fibro-myoma of the ovary. The tissues of which the tumour is made up exist in the organ which it attacks.

Putting aside a case which I have already reported ("Clinical and Pathological Observations on Tumours of the Ovary," p. 97), and a second case where a fibro-cystic tumour proved on microscopical examination to be fibro-myomatous, but where there was a little doubt about its

ovarian origin ('Trans. Obstet. Soc.,' vol. xxix, p. 513), I come to an apparently undoubted specimen of fibro-myoma of the ovary. The tumour was removed by Mr. Meredith from a woman aged forty who had dysmenorrhœa for a year, without any definite symptoms of ovarian disease. The duration of the growth was quite uncertain and the patient was in good health a year after its removal. The specimen is preserved in the museum of St. Bartholomew's Hospital, Path. Ser., No. 2925 *a*. It is an oblong tumour, measuring about four inches in its long diameter; the relations of the tube and broad ligament leave no doubt that the tumour replaces the ovary. In the museum catalogue it is stated, quite incorrectly in my opinion, that "the structure of the tumour is exactly similar to that of a normal ovary, closely resembling a spindle-celled sarcoma."

I was not aware that a normal ovary closely resembled a spindle-celled sarcoma, and the structure of this tumour is very dissimilar to that of a normal ovary. Some or all of its histological elements no doubt exist in the ovary, but not arranged in the same fashion. Fig. 7 is drawn from a section of the tumour kindly lent to me by Dr. Griffith. A stroma of wavy fibrous tissue is conspicuous. Intimately blended with the wavy fibres are cells with elongated nuclei. They bear all the characters of muscle-cells. They are much larger than the nuclei in the fibroma of the ovary (fig. 5) and are not of the form and arrangement of the sarcoma cells in fig. 6. I see no reason why they should not be considered as muscle-cells. They are arranged precisely like muscle-cells in a fibro-myoma of the uterus (fig. 4). Those who object and say that the cells in fig. 7 are not muscle-cells but cells of the same form must take the responsibility of proving from wider evidence that there are plain muscle-cells and fusiform bodies of precisely the same appearance which are not muscle-cells.

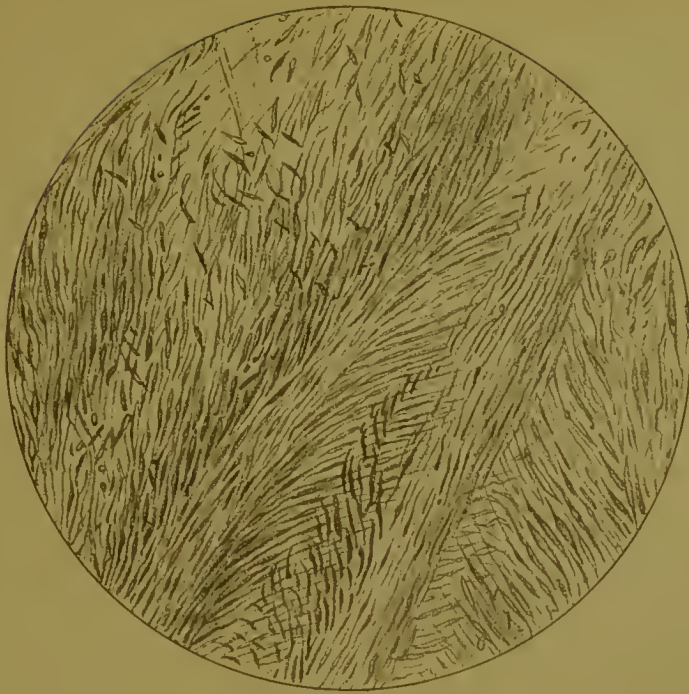
The sarcoma-cells in fig. 6 and the connective-tissue nuclei in fig. 5 are, as these drawings show, not identical with the cells in fig. 7, which cells most resemble those of

plain muscular tissue. At the same time, all three varieties of cell agree in one character. They are closely connected with the fibrils of the stroma. In this they show a common connective-tissue origin, which nobody will dispute in the case of the fibroma and sarcoma and few would reject in the case of the myoma.

We may conclude then, that a careful study of the histological features of uterine "fibroids" and of certain innocent solid tumours of the ovary teaches us that, however rare, fibroma and fibro-myoma of the ovary are not unknown, and that according to the light of general pathology, and the comparison of the known with the uncertain, muscle-cells, the fusiform cells of fibrous tissue and the specific spindle-cells of a sarcoma may, in many cases, be distinguished from each other.

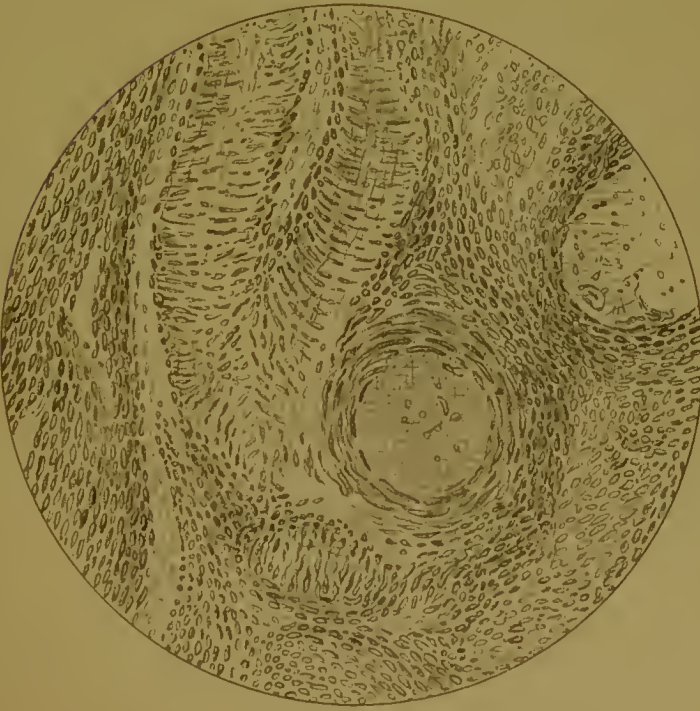
*The Ovary in Myoma of Uterus - See
Van Meersdervoort. Ned. Tijdschrift
voor Verloskunde en Gynaecologie.
Aft. I. 1897 - 1898. Dr. G. J. de Vries.
Vol. II 1898. p. 171 (July-Aug.)*

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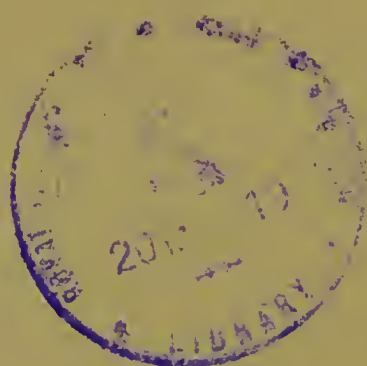


Myometrium of the Ovarian ligament
Showing muscle cells intertwined with any other structure

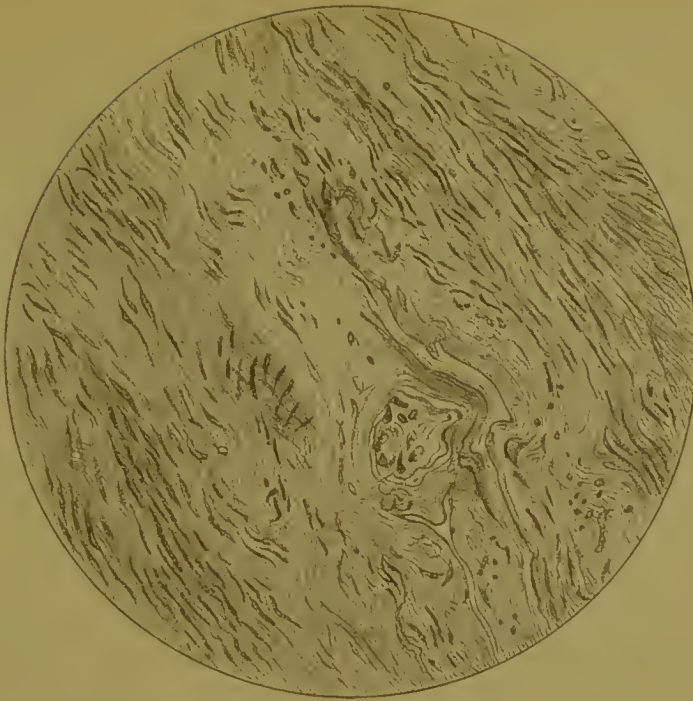
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Section of the Uterus of a child aged 11.
Two large vessels run across the field from the right to the centre, where another vessel is seen in transverse section. The muscle cells of their middle coats are well displayed. Between the vessels are seen the stout, short nuclei of the young muscle cells of the uterine tissue.

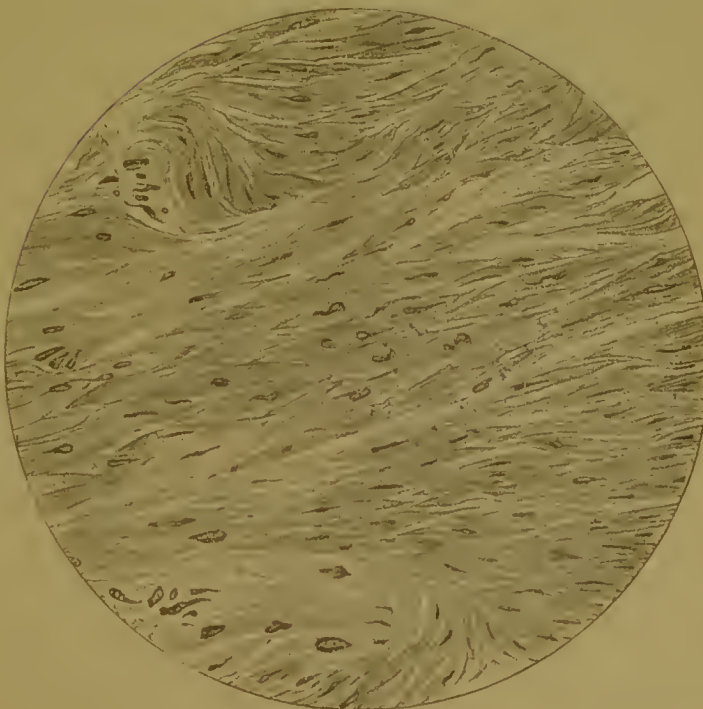


4.



Fibro myoma of the Uterus

In some parts of the field the muscle cells & the fibrous tissue lie separate, in others they are closely blended



Myoma of a pregnant Uterus

Showing extreme hypertrophy of the muscle cells



6

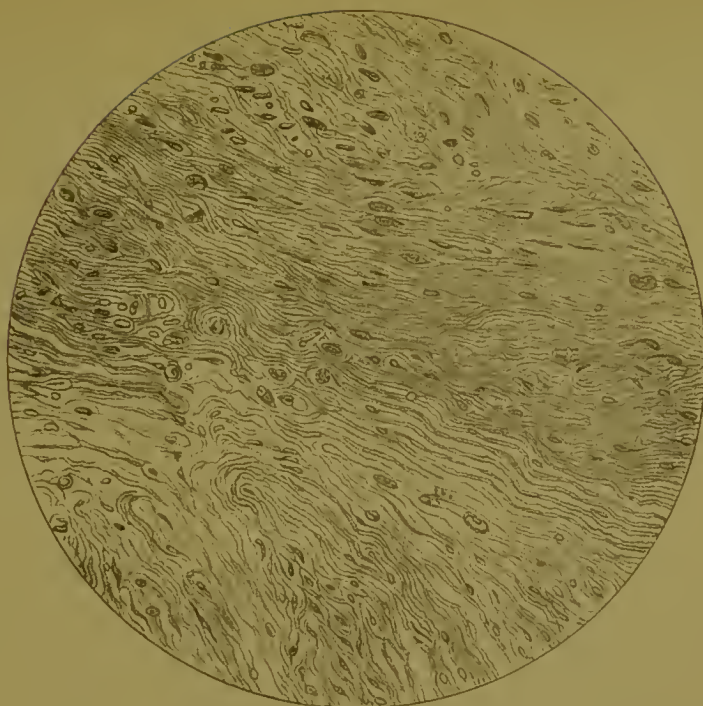
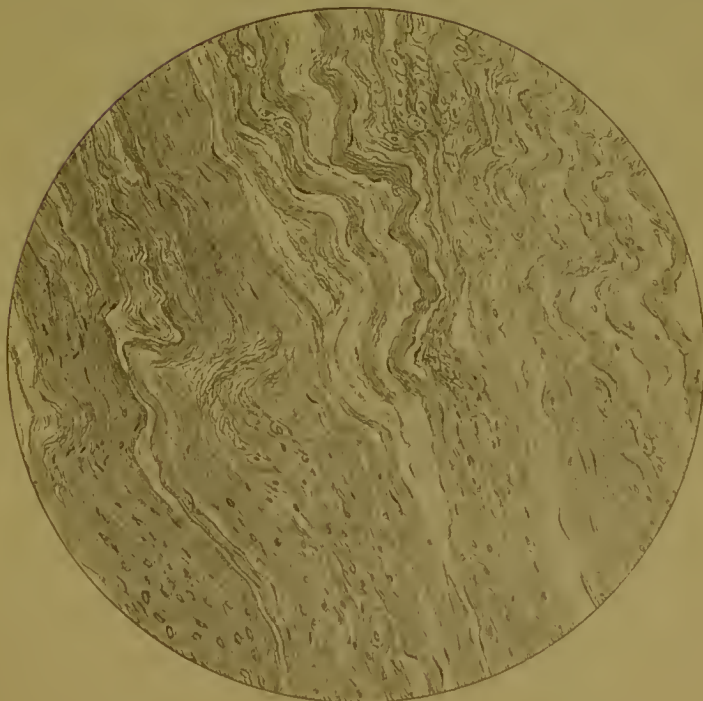


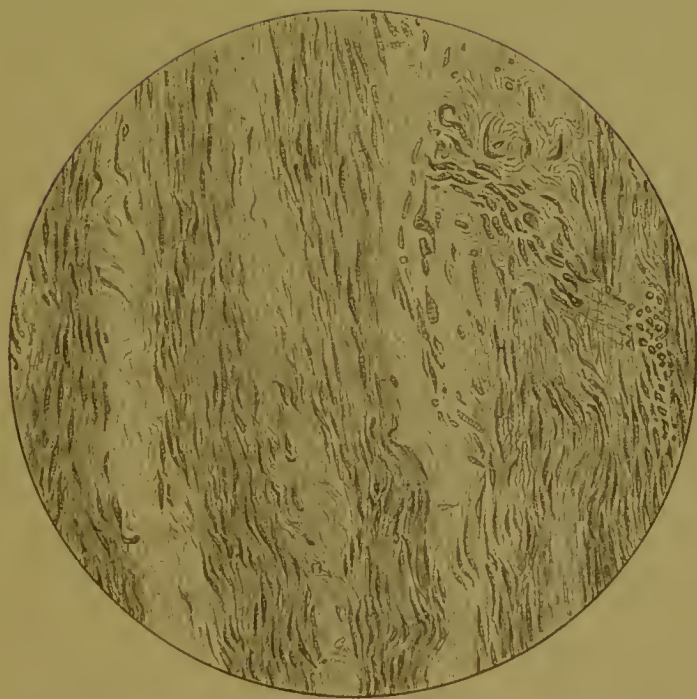
Diagram 1 of the Ovary
 from a portion where much fibrous tissue was
 blended with spindle cells

5



Fibroma of the Ovary
 The basis of pure fibrous tissue bear small fusiform
 nuclei & isolated small cells with oval nuclei





Fibromyoma of the Ovary.

Structures resembling the muscle-cells in Fig. 4 (fibromyoma of the uterus) are mixed with bands of fibrous tissue

